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DDT Synergists. The Synthesis and Prop-
erties of Some 2,2-Difluoro-1,1-diarylethanol
and 2-Fluoro-1,1-diarylethenes

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DDT Synergists. The Synthesis and Properties of Some 2,2-Difluoro-1,1-diarylethanols and 2-Fluoro-1,1-diarylethenes

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A number of 2,2-difluoro-1,1-diarylethanols have been prepared by treatment of ethyl difluoroacetate with aryl Grignard reagents. These alcohols were reduced to the corresponding ethanes, which, in turn, were dehydrofluorinated to yield a series of 2-fluoro-1,1-diarylethenes. Some preliminary results of a study of the insecticidal power and of the synergistic activity of these compounds with DDT are reported.

In connection with studies on synergism of DDT, we undertook the preparation of a number of diarylethanols containing fluorine in the ethane moiety. While this program was in progress, Kaluszyner and coworkers^{2,3} reported the preparation

of a number of 2,2,2-trifluoro-1,1-diarylethanols from the reaction of aryl Grignard reagents with ethyl trifluoroacetate. This paper summarizes the results obtained in this laboratory from the treat-

(1) Inquiries should be addressed to this author at Department of Chemistry, Boston College, Chestnut Hill, Mass.

(2) A. Kaluszyner, S. Reuter, and E. D. Bergmann, *J. Am. Chem. Soc.*, **77**, 4164 (1955).

(3) R. Mechoulam, S. Cohen, and A. Kaluszyner, *J. Org. Chem.*, **21**, 801 (1956).

TABLE I
 2,2-DIFLUORO-1,1-DIARYLETHANOLS $\text{Ar}_2\text{C}(\text{OH})\text{CHF}_2$

Ar	B.P., °C.	Mm.	Yield, %	Formula	Color with Concd. H_2SO_4	Analyses			
						Carbon		Hydrogen	
						Calcd.	Found	Calcd.	Found
Phenyl ^a	110–111	0.15	64	$\text{C}_{14}\text{H}_{12}\text{F}_2\text{O}$	Orange	71.78	72.1	5.17	5.1
<i>p</i> -Fluorophenyl ^b	99–100	0.05	43	$\text{C}_{14}\text{H}_{10}\text{F}_4\text{O}$	Red-orange	62.23	62.5	3.73	3.7
<i>p</i> -Chlorophenyl ^c	130–136	0.20	53	$\text{C}_{14}\text{H}_9\text{Cl}_2\text{F}_2\text{O}$	Cherry-red	55.47	55.63	3.33	3.47 ^d
<i>p</i> -Bromophenyl ^e	153–164	0.17	40 ^f	$\text{C}_{14}\text{H}_9\text{Br}_2\text{F}_2\text{O}$	Red	42.88	42.9	2.57	2.4 ^g

^a n_D^{25} 1.5593. ^b n_D^{25} 1.5276. ^c n_D^{25} 1.5780. ^d Calcd.: Cl, 23.40. Found: Cl, 23.94. ^e n_D^{25} 1.6039. The compound crystallized in the form of thick prisms after standing six months, m.p. 54.5–56.0°. ^f A large amount of tarry residue was obtained on distillation of the crude material. ^g Calcd.: Br, 40.77. Found: Br, 40.5.

 TABLE II
 2,2-DIFLUORO-1,1-DIARYLETHYL ACETATES $\text{Ar}_2\text{C}(\text{OCOCH}_3)\text{CHF}_2$

Ar	M.P., °C.	Recryst. Solvent	Yield, %	Formula	Analyses			
					Carbon		Hydrogen	
					Calcd.	Found	Calcd.	Found
Phenyl	51.0–52.0	Methanol	80	$\text{C}_{16}\text{H}_{14}\text{F}_2\text{O}_2$	69.55	69.6	5.11	5.1
<i>p</i> -Fluorophenyl ^a	89	$\text{C}_{16}\text{H}_{12}\text{F}_4\text{O}_2$	61.53	61.8	3.87	3.9
<i>p</i> -Chlorophenyl	86.0–86.8	Pet. ether	82	$\text{C}_{16}\text{H}_{11}\text{Cl}_2\text{F}_2\text{O}_2$	55.67	55.8	3.50	3.3
<i>p</i> -Bromophenyl	80.0–80.5	Methanol-water	86	$\text{C}_{16}\text{H}_{11}\text{Br}_2\text{F}_2\text{O}_2$	44.25	44.3	2.79	2.9 ^b

^a Resisted all attempts to induce crystallization; isolated as very viscous oil by molecular distillation at 80° and 0.1 mm., n_D^{25} 1.5158. ^b Calcd.: Br, 36.80. Found: Br, 36.8.

ment of ethyl difluoroacetate with various aryl-magnesium bromides.

Phenylmagnesium bromide and its derivatives carrying either chlorine, bromine, or fluorine in the *p*-position reacted readily at 0° with ethyl difluoroacetate to yield the expected 2,2-difluoro-1,1-diarylethanols, $\text{Ar}_2\text{C}(\text{OH})\text{CHF}_2$. As Table I shows, the yields of the ethanols varied from 40 to 64%, depending upon the substituent in the aromatic ring. The yields were lowered when the reaction was carried out at room temperature or above. All of the tertiary alcohols were isolated as colorless or faintly straw-colored, high-boiling, viscous oils; only the *p*-bromo compound crystallized. The ethanols gave characteristic colors with concentrated sulfuric acid and displayed the typical O-H stretching band at 3590 cm^{-1} in the infrared (carbon tetrachloride solution). The alcohols were further characterized by conversion to the acetates (Table II).

The ethanols were reduced to the corresponding ethanes in good yield (Table III) by heating under reflux for ten days with phosphorus and iodine in aqueous acetic acid.⁴ It was interesting to note that the ethanes, unlike the ethanols, were rather mobile oils and all of them, except for 2,2-difluoro-1,1-bis-(*p*-fluorophenyl)ethane, crystallized readily. The ethanes, as expected, gave no coloration with concentrated sulfuric acid and their infrared spectra showed complete absence of hydroxyl.

The ethanes were converted smoothly to the corresponding 2-fluoro-1,1-diarylethenes (Table IV) when refluxed with 2% ethanolic potassium hydrox-

ide. The clean-cut nature of this dehydrofluorination is interesting in view of the report³ that treatment of 2,2,2-trifluoro-1,1-diarylethanols with ethanolic potassium hydroxide or sodium ethoxide results in alcoholysis of the trifluoromethyl group. All of the ethenes displayed very intense absorption in the infrared at 1630 cm^{-1} (carbon tetrachloride solution), indicative of the presence of $> \text{C} = \text{C} <$ conjugated with an aromatic ring.⁵ Furthermore, these compounds gave positive tests with bromine in carbon tetrachloride and with potassium permanganate in water-acetone solution, whereas the ethane progenitors were completely unreactive toward these diagnostic reagents.

Dimroth and Bockemüller had previously described⁶ the preparation of 2-fluoro-1,1-diphenylethene and claimed this compound was a solid melting at 93.5°. Our preparation, in contrast, is a mobile oil at room temperature and, moreover, as Table IV reveals, all of the *p*-halo substituted derivatives melt below 93.5°. These investigators prepared their sample of this ethene by dehydrofluorinating with ethanolic potassium hydroxide 1,2-difluoro-1,1-diphenylethane, which was claimed to have been formed by treating 1,1-diphenylethene with a mixture of lead tetraacetate and hydrogen fluoride in chloroform. The isolation of desoxybenzoin as a by-product from the latter reaction suggests that possibly the structure believed by Dimroth and Bockemüller to be 2-fluoro-1,1-di-

(5) L. J. Bellamy, *The Infra-red Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, 1954, p. 36.

(6) O. Dimroth and W. Bockemüller, *Ber.*, 64, 516 (1931).

(4) F. A. Gunther and R. C. Blinn, *J. Am. Chem. Soc.*, 72, 4282 (1950).

TABLE III
 2,2-DIFLUORO-1,1-DIARYLETHANES $\text{Ar}_2\text{CHCHF}_2$

Ar	M.P., °C.	Recryst. Solvent	Yield, %	B.P., °C.	Mm.	Formula	Analyses			
							Carbon		Hydrogen	
							Calcd.	Found	Calcd.	Found
Phenyl	38.5-39.5	Ethanol	91	85	0.15	$\text{C}_{14}\text{H}_{12}\text{F}_2$	77.05	76.8	5.54	5.5
<i>p</i> -Fluorophenyl ^a	90	79-80	1.5 ^b	$\text{C}_{14}\text{H}_{10}\text{F}_4$	66.14	66.6	3.97	4.0
<i>p</i> -Chlorophenyl	37.5-38.5	Methanol-water	90	110-118	0.08	$\text{C}_{14}\text{H}_{10}\text{Cl}_2\text{F}_2$	58.56	58.8	3.51	3.5 ^c
<i>p</i> -Bromophenyl	42.0-42.8	Methanol	89	$\text{C}_{14}\text{H}_9\text{Br}_2\text{F}_2$	44.70	44.80	2.68	2.8 ^d

^a Could not be obtained crystalline. ^b n_D^{25} 1.5179. ^c Calcd.: Cl, 24.69. Found: Cl, 24.8. ^d Calcd.: Br, 42.48. Found: Br, 42.5.

 TABLE IV
 2-FLUORO-1,1-DIARYLETHENES $\text{Ar}_2\text{C}=\text{CHF}$

Ar	M.P., °C.	B.P., °C.	Mm.	Recryst. Solvent	Yield, %	Formula	Analyses			
							Carbon		Hydrogen	
							Calcd.	Found	Calcd.	Found
Phenyl ^a	...	77	0.05	...	91	$\text{C}_{14}\text{H}_{11}\text{F}$	84.82	85.1	5.59	5.7
<i>p</i> -Fluorophenyl	32-33	81-82	1.0 ^b	Methanol	93	$\text{C}_{14}\text{H}_9\text{F}_3$	71.79	71.9	3.87	4.0
<i>p</i> -Chlorophenyl	78.0-79.5	Methanol	85	$\text{C}_{14}\text{H}_9\text{Cl}_2\text{F}$	62.91	62.9	3.39	3.4 ^c
<i>p</i> -Bromophenyl	84.2-85.2	Methanol	85	$\text{C}_{14}\text{H}_9\text{Br}_2\text{F}$	47.20	47.0	2.55	2.4 ^d

^a Crystallizes in refrigerator, n_D^{25} 1.5872. ^b n_D^{25} 1.5481. ^c Calcd.: Cl, 26.53. Found: Cl, 26.4. Calcd.: F, 7.11. Found: F, 6.96. ^d Calcd.: Br, 44.86. Found: Br, 44.7.

phenylethene is actually an isomer prepared by the dehydrofluorination of an unexpected rearranged product. Further support of the validity of our structure, in addition to the evidence cited above, was obtained by oxidizing the compound by chromic anhydride in acetic acid to benzophenone, isolated, in excellent yield, as the 2,4-dinitrophenylhydrazone.

EXPERIMENTAL⁷

The preparation of 2,2-difluoro-1,1-diphenylethanol illustrates the general procedure used in obtaining the substituted ethanols. Freshly purified ethyl difluoroacetate (20.0 g., 0.16 mole), diluted with an equal volume of ether, was added with stirring in the course of 1 hr. to the ice-cold Grignard reagent prepared from 10.7 g. (0.44 g.-atom) of magnesium turnings and 69.0 g. (0.44 mole) of bromobenzene in 100 ml. of ether. Stirring and cooling in the ice-bath were maintained for 2 hr. after completion of the addition of the ester. The reaction mixture, after standing at room temperature overnight, was treated, while stirring and cooling, with saturated ammonium chloride, prepared by shaking 40 g. of the salt with 100 ml. of water. The yellow suspension was filtered with suction through a sintered-glass funnel, the filter cake was washed with ether, and the combined ethereal extract washed twice with water before being dried over sodium sulfate. Evaporation of the ether yielded a dark orange oil which was diluted with an equal volume of methanol and refrigerated at -35° for 2 days in order to allow the traces of biphenyl to crystallize. Filtration of the mixture followed by steam distillation of the filtrate (2 l. of distillate was collected and discarded) gave a product which was essentially free of starting material and derived

products. The oily residue was dissolved in ether and dried over sodium sulfate. Removal of the solvent and distillation of the residue afforded 24.0 g. (64%) of the product, b.p. $110-111^\circ$ at 0.15 mm., as a colorless oil.

The 2,2-difluoro-1,1-diarylethyl acetates were prepared either by heating the alcohol with acetic anhydride in the presence of catalytic amounts of concentrated sulfuric acid⁸ or by allowing the alcohol to stand at room temperature for several hours with a mixture of acetic acid-trifluoroacetic anhydride.⁹ The products, isolated in the usual way, showed the characteristic carbonyl absorption band at 1750 cm^{-1} in carbon tetrachloride solution.

Reduction to 2,2-difluoro-1,1-diarylethanes was effected by heating 8.0-10.0 g. of the appropriate alcohol under reflux for 10 days with a mixture of 3.5 g. of red phosphorus, 1.27 g. of iodine, 50 ml. of glacial acetic acid, and 1.0 ml. of water. The cooled reaction mixture was filtered with suction directly into a separatory funnel containing 300 ml. of 2.5% sodium bisulfite. The oily suspension was neutralized by adding portions of solid sodium bicarbonate with intermittent shaking and was then extracted with ether. The ether extract was dried over sodium sulfate after being washed with water. Removal of the ether and distillation of the residue *in vacuo* yielded a colorless, mobile oil, which spontaneously crystallized, except in the case of the *p*-fluoro compound.

General procedure for the preparation of 2-fluoro-1,1-diarylethanes. The substituted ethane (2.2 g.) was heated under reflux for 2.5 hr. with 60 ml. of 2% ethanolic potassium hydroxide. The solvent was removed under reduced pressure and the residue extracted with several portions of ether. The combined ethereal extract was washed with water and dried over magnesium sulfate. Removal of the ether afforded a colorless oil which was distilled at diminished pressure. Of this series, only 2-fluoro-1,1-diphenylethene could not be obtained crystalline at room temperature.

Oxidation of 2-fluoro-1,1-diphenylethene. A 281-mg. quantity of this compound was heated under reflux for 3 hr. with a mixture of 550 mg. of chromium trioxide, 15 ml. of glacial acetic acid, and 3 drops of water. The green solution was

(7) Melting points are corrected and boiling points are uncorrected. Infrared measurements were made using a Baird double beam recording spectrophotometer equipped with a sodium chloride prism. The majority of the elemental analyses were performed by Dr. Carol K. Fitz, Needham Heights, Mass.

(8) L. F. Fieser, *Experiments in Organic Chemistry*, 2nd. ed., D. C. Heath and Company, Boston, 1941, p. 397.

(9) J. M. Tedder, *Chem. Revs.*, 55, 787 (1955).

poured onto cracked ice, 30 ml. of water was added, and the mixture was extracted twice with 50-ml. portions of ether. The combined extract was washed successively with water, 10% potassium carbonate (20 ml.), and water. After drying over sodium sulfate and evaporation of the ether the residue was dissolved in 8 ml. of ethanol and treated with 2,4-dinitrophenylhydrazine. Recrystallization of the precipitate from glacial acetic acid gave orange needles, m.p. 239–240° (recorded¹⁰ m.p. 238–239°). A mixed melting point with an authentic specimen of benzophenone 2,4-dinitrophenylhydrazone showed no depression. The infrared spectra of the two samples (chloroform solution) were totally superimposable.

Biological results. In tests with house flies, the ethanes

carrying *p*-chloro- and *p*-bromo-substituents were the most active insecticides of the entire series of compounds; the corresponding ethanols were somewhat less active. None of the acetates and ethenes displayed significant insecticidal activity.

On the other hand, the *p*-chloro- and *p*-bromo-substituted ethanes, ethanols, and acetates proved to be excellent synergists for DDT in tests with DDT-resistant house flies. The synergistic activity of these compounds surpassed that of 1,1-bis(*p*-chlorophenyl)ethanol (DMC), one of the most effective DDT synergists.¹¹ The ethenes were less effective. A detailed report of this study will be published elsewhere.

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(10) E. H. Huntress and S. P. Mulliken, *Identification of Pure Organic Compounds*, Order I, John Wiley and Sons, Inc., New York, 1941, p. 363.

(11) R. L. Metcalf, *Organic Insecticides, Their Chemistry and Mode of Action*, Interscience Publishers, Inc., New York, 1955, p. 368.